2019 NCCMP Annual Conference
Prescription Drug Discussion

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We are enthusiastic about demonstrating the areas in which we can be of assistance.

**Discussion Topics**

1. New Drug Overview
2. Generics and Biosimilar Drugs
3. Gene Therapy
4. Drugs in Development
5. Summary & Options
6. Q&A
New drug development is increasingly focused around rare disease.

Cost of new drugs continues to increase along with concern over how to pay for these treatments.

Ongoing legislative debate on how to reduce drug prices.

January 2019, three dozen manufacturers announce raising prices on 250+ prescription drugs.

78% of all health care cost is lifestyle/behavior related.

Chart is showing novel new drugs: Novel drugs are often among the more innovative products in the marketplace, and/or help advance clinical care by providing therapies never before marketed in the United States.

2019 New drugs approved through September 16.
Oncology (16 of the 59 new approvals)

- Oncology drugs are used to treat a variety of cancers and represent the largest class of drugs approved.

- Examples of notable novel Oncology approvals for 2018 include:
  - Braftovi (encorafenib) and Mektovi (binimetinib) in combination to treat patients with metastatic melanoma.
  - Vitrakvi (larotrectinib) to treat adult and pediatric patients whose cancers have a specific genetic feature (biomarker).

Drugs for Rare Diseases (22 of the 59 new approvals)

- These drugs treat rare or “orphan” diseases that affect 200,000 or fewer Americans. Patients with rare diseases often have few or no drugs available to treat their conditions.

- Examples of drugs that advance the care of patients with rare diseases approved in 2018 include:
  - Epidiolex (cannabidiol), for the treatment of two rare and severe forms of epilepsy: Lennox-Gastaut syndrome and Dravet syndrome, in individuals two years of age and older.
  - Palynziq (pegvaliase-pqpz), Injection is the first FDA-approved enzyme substitution therapy designed to address the underlying cause of phenylketonuria (PKU), a rare and genetic brain-threatening condition.
New Drugs - 2019

- **Skyrizi** (risankizumab-rzaa)
  - Moderate to severe plaque psoriasis
  - Two injections every 12 weeks
  - $59,000 per patient per year

- **Rinvoq** (upadacitinib)
  - Moderately to severely active rheumatoid arthritis.
  - Taken daily as a pill.
  - $59,000 per patient per year

- **Zulresso** (brexanolone)
  - First treatment for postpartum depression in adult women.
  - 60 hour infusion given in hospital.
  - $34,000 for the drug + hospital cost

- **Vyleesi** (bremelanotide)
  - Low sex drive in women
  - Injection that needs to be administered at least 45 minutes before anticipated sexual activity.

- **Jeuveau** (prabotulinumtoxinA-Xvfs)
  - Temporary improvement in the appearance of moderate to severe glabellar lines.

- 9 of 27 approvals are for various forms of Cancer.

- One new drug each for
  - Multiple Sclerosis
  - Parkinson’s Disease
  - Pneumonia
  - Irritable bowel syndrome
  - Flat worms
FDA: Record-setting year for generic drug approvals

• 1,027 new generic drugs approved
  – 843 full approvals
  – 184 “tentative” approvals
• 80 are first generic alternatives
• Priority review for up to third alternative to a brand-name drug

Generics saved consumers $1.67 trillion over the last decade

Source: U.S. Food and Drug Administration
Expected New Generics: 2019

- Expected new generics based on most current market intelligence. All subject to FDA approval and depending on drug legal challenges from brand manufacturer to block generic approval.
- It is important to note that generics may be approved but there is no requirement for a manufacturer or multiple manufacturers to produce the generic.

<table>
<thead>
<tr>
<th>Anticipated Availability</th>
<th>Brand</th>
<th>Generic Name</th>
<th>Common Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 2019</td>
<td>Latuda</td>
<td>Lurasidone</td>
<td>Bipolar Depression</td>
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<tr>
<td>Q1 2019</td>
<td>Zyclara</td>
<td>Imiquimod cream</td>
<td>Actinic keratoses</td>
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<tr>
<td>Q1 2019</td>
<td>Herceptin</td>
<td>Trastuzumab</td>
<td>Breast cancer</td>
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<tr>
<td>Q1 2019</td>
<td>Restasis</td>
<td>Cyclosporine ophthalmic emulsion</td>
<td>Moderate to severe dry eyes</td>
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<tr>
<td>Q1 2019</td>
<td>Gilenya</td>
<td>Fingolimod</td>
<td>Multiple sclerosis</td>
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<tr>
<td>Q1 2019</td>
<td>Ranexa</td>
<td>Ranolazine</td>
<td>Angina</td>
</tr>
<tr>
<td>Q1 2019</td>
<td>Solodyn</td>
<td>Minocycline extended-release tablet</td>
<td>Acne</td>
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<tr>
<td>Q1 2019</td>
<td>AzaSite</td>
<td>Azithromycin 1% ophthalmic solution</td>
<td>Bacterial conjunctivitis</td>
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<tr>
<td>Q1 2019</td>
<td>Emend</td>
<td>Fosaprepitant injection</td>
<td>Nausea and vomiting</td>
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<tr>
<td>Q1 2019</td>
<td>Faslodex</td>
<td>Fulvestrant</td>
<td>Breast Cancer</td>
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<tr>
<td>Q2 2019</td>
<td>Exjade</td>
<td>Deferasirox tablets for oral suspension</td>
<td>Iron Toxicity</td>
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<td>Q2 2019</td>
<td>Vesicare</td>
<td>Solifenacin succinate</td>
<td>Overactive bladder</td>
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<tr>
<td>Q2 2019</td>
<td>Sporanox</td>
<td>Itraconazole solution</td>
<td>Antifungal</td>
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<tr>
<td>Q2 2019</td>
<td>Uloric</td>
<td>Febuxostat</td>
<td>Gout</td>
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<tr>
<td>Q3 2019</td>
<td>Lyrica</td>
<td>Pregabalin</td>
<td>Fibromyalgia</td>
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<tr>
<td>Q3 2019</td>
<td>Edluar</td>
<td>Zolpidem sublingual tablet</td>
<td>Insomnia</td>
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<tr>
<td>Q3 2019</td>
<td>Factive</td>
<td>Gemifloxacin</td>
<td>Antibiotic</td>
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<tr>
<td>Q3 2019</td>
<td>Zubsolv</td>
<td>Buprenorphine/Naloxone sublingual tablet</td>
<td>Narcotic dependence</td>
</tr>
<tr>
<td>Q4 2019</td>
<td>Treanda</td>
<td>Bendamustine (powder)</td>
<td>Chronic lymphocytic leukemia</td>
</tr>
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</table>
Biosimilars are “generic-like” versions of biologic drugs. Biologic drugs are manufactured using a living organism, which makes it difficult to produce exact copies like other generic drugs.

There have been several biosimilar drugs approved, however, only a few are available due to legal disputes, manufacturing issues and provider contracts.

Overall list price for biosimilars may be up to 20% less. However contracts with medical plans and PBMs for brand products may offset this price advantage.
Breaking Gene Therapy News

Zolgensma: A Remarkable New Treatment, An ICER Analysis, And A Poorly Justified Price

By Robert J. Smith
JUNE 19, 2019

OBJECTIVE: In both sets of alleles, the coding region for F9 gene, which is responsible for the production of the blood clotting factor IX, is disrupted, leading to severe hemophilia A. Zolgensma is the first approved gene therapy for hemophilia A, which is characterized by bleeding tendencies in the affected areas. Zolgensma is a one-time treatment that delivers a healthy copy of the F9 gene to the patients' muscles, allowing them to produce the factor IX protein. The treatment is typically given to infants aged 0 to 12 months, with the option to continue the dosing up to 18 months.

In May 2019, Novartis released the results of the Zolgensma trial, which showed a significant improvement in muscle function in both treated and untreated patients. The results were promising, with more than 50% of patients showing a noticeable improvement in muscle function. However, the treatment is not without its challenges. One major concern is the high cost of the treatment, which can range from $1.2 million to $2.1 million per patient. This high cost has raised questions about the affordability of the treatment and its long-term effectiveness.

The high cost of Zolgensma has led to debates about whether it is justified. Critics argue that the cost is not justified by the benefits it provides, especially given the potential for alternative treatments. The ICER analysis provides an in-depth look at the costs and benefits of Zolgensma, offering insights into whether the treatment is a cost-effective option for patients with hemophilia A.

The Wall Street Journal

High Hopes for a Gene Therapy Come With Fears Over Cost

Luxturna can improve sight for children and others with a rare eye condition, but costs: nearly $1 million—the industry is reckoning with how to pay for such treatments as more become available

By Saniya Iyengar
Updated Sept. 24, 2019 4:33 pm ET

Just 4 years old, Caspian Soto uses a cane and headlamp to help him see when he walks. He can’t see in dark places like aquariums or movie theaters. He’s never seen the stars.

Caspian was born with a rare, inherited eye disorder called Leber congenital amaurosis, which results in the progressive deterioration of the retina, the tissue at the back of the eye that detects light and color. He could lose all vision by the time he’s a teenager.
The concept of gene therapy was introduced after the development of recombinant DNA technology. Researchers first suggest gene therapy as a treatment for genetic diseases in a paper in the journal Science but they oppose its use in humans “for the foreseeable future,” pending greater understanding of the technology.

The first gene therapy trial on humans was performed by researchers at the National Institutes of Health. A four-year old girl with severe immunodeficiency became the first patient to undergo gene therapy.

Cases of leukemia are diagnosed in French children undergoing gene therapy for genetic immunodeficiency in a further blow to the field.

European patient Jesse Gelsinger dies following a gene therapy experiment, setting the field back several years as U.S. regulators put some key experiments on hold.

British doctors carry out the world’s first operation using gene therapy to treat a serious sight disorder caused by a genetic defect.

Gene therapy shows promise in clinical trials for inherited blood disorders, certain types of progressive blindness and HIV.

In 2017, the United States finally approved its first gene therapy, a CAR-T.
Gene Therapy

What to know about Gene Therapy

- Gene Therapy is a novel approach to treat, cure, or ultimately prevent disease by changing the expression of a person’s genes.
- In general, gene therapy involves replacing a gene that causes a medical problem with one that does not, adding genes to help the body fight or treat disease, or turning off genes that cause medical problems.
- Cost of treatment in excess of $500,000 per patient.
- Current treatments for Leukemia, Rare Genetic Blindness and Spinal Muscular Atrophy (SMA).
More than 400 therapies are in development pipeline.

Targeting primarily rare disease with limited to no treatment options.

Technology advancements are allowing the development of highly targeted therapies.

Growing concern over cost, payment models and commercial success.

Table shows Gene Therapies in late stage development with targeted release dates between 2020 and 2022.
The FDA Accelerated Approval Program allows faster approval of drugs for serious conditions that fill an unmet medical need.

The faster approval relies on use of surrogate endpoints or something that is thought to predict clinical benefit.

Drug approvals typically require clinical trials with endpoints that demonstrate a clinical benefit.

Surrogate endpoints typically require less time, and in the case of a cancer patient, it is much faster to measure a reduction in tumor size, for example, than overall patient survival.

Drugs approved under the FDA Accelerated Approval Program still need to be tested in clinical trials using endpoints that demonstrate clinical benefit, and those trials are known as phase 4 confirmatory trials.

If the drug later proves unable to demonstrate clinical benefit to patients, the FDA may withdraw approval.
Researchers reviewed 93 cancer drug uses for which accelerated approval was granted between 1992 and 2017.

The researchers found that only 19 of those drug uses ended up demonstrating improvements in overall patient survival in subsequent confirmatory trials.

Source: IQVIA Institute, Mar 2018
Chart notes: A New Active Substance (NAS) is a new molecular or biologic entity or combination where at least one element is new. Medicines listed by first launch year and listed alphabetically by molecular name.
Report: Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022, Apr 2018
Leaky Gut Syndrome

Faulty tight junction

Healthy tight junction

Undigested food particles, microorganisms and toxines

Blood capillaries

INFLAMMATORY, IMMUNOLOGICAL, AUTOIMMUNE AND NEOPLASTIC REACTIONS
Drug spend that can be related to Leaky Gut Syndrome

2018 Spend (Billions)

- Diabetes: $60.6
- Oncology: $58.4
- Auto-Immune Disease: $54.1
- GI Products: $8.7
- Dermatologicals: $8.7
Drug innovation continues at a rapid pace primarily focused on rare diseases with limited to no treatment options.

Drugs are coming to market faster than ever before with rising concern about overall effectiveness.

Saving opportunities still exist with generics and biosimilar drugs.

Plan sponsors should consider:
- Plan design options to accommodate new drugs
- Formularies driving to lowest net cost
- Exclusion of high cost low value drugs
- Clinical utilization management programs
- Managing drug spend through both the pharmacy plan and medical plan
- Alternative treatment programs beyond drug therapy
- Using data analytics to identify potential risk of new therapy impact

Be prepared to continuously evaluate new drugs and treatments!!
Thank you

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